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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/763,824

02/27/2001

David J Squirrel

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05/16/2006

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/763,824

Applicant(s)

SQUIRRELL ET AL.

Examiner

David J. Steadman

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– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 67-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/15/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

- [1]** Claims 67-85 are pending in the application.
- [2]** Applicant's amendment to the claims, filed on 2/21/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3]** Applicant's amendment to the specification, filed on 2/21/2006, is acknowledged.
- [4]** Receipt of a letter filed on 9/27/2005 requesting initialing of the reference of Ye et al. in the information disclosure statement filed on 4/15/2005 is acknowledged.
- [5]** Receipt of a sequence listing in computer readable form (CRF), a paper copy thereof, a statement of their sameness, a statement that no new matter has been added to the specification by the paper copy of the sequence CRF, and an amendment to the specification directing entry of the sequence listing, all filed on 2/21/2006, is acknowledged.
- [6]** Applicant's arguments filed on 2/21/2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [7]** The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Examiner Comment/Clarification

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[8] A substitute sequence listing is filed with the instant response, adding the sequence of SEQ ID NO:37, which, according to applicant, is the wild-type sequence of *Photinus pyralis* luciferase. The sequence appears to have been incorporated from PCT/GB98/01026, which is properly incorporated by reference at p. 12, lines 14-15 of the specification.

Information Disclosure Statement

[9] The examiner inadvertently failed to initial beside the reference of Ye et al. in the PTO-1449 attached to the Office action mailed on 9/19/2005. A copy of Form PTO-1449 correcting this deficiency is attached to the instant Office action.

Claim Objections

[10] Claims 67 and 71 are objected to as reciting non-elected subject matter. It is suggested that applicant remove the non-elected subject matter from the claims. Claims 67 and 71 are being examined only to the extent the claims read on the elected subject matter. As noted in the Office action mailed on 12/15/2004, the elected invention is drawn to (in relevant part) the special technical feature of a variant of *Photinus pyralis* luciferase having mutation at position 214 and having increased thermostability. While applicant asserts "[t]he claims are directed to the elected invention" in the instant response, it is noted that the claims are also directed to non-elected inventions. See the requirement for restriction in the Office action mailed on 1/30/2004, applicant's election,

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filed on 3/1/2004, and the decision on petition mailed on 8/26/2005. It is suggested that applicants amend the claims so that they no longer recite non-elected subject matter.

[11] Claim 78 is objected to as being grammatically incorrect in the recitation of "cells according to claim 77," as claim 77 is drawn to a singular "cell." It is suggested that applicant replace "cells" in claim 78 with "a cell."

Claim Rejections - 35 USC § 112, Second Paragraph

[12] Claims 79 and 85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] The term "an improvement" in claim 79 is unclear absent a statement defining to what the improved bioluminescent assay is being compared. The term "an improvement" is a relative term and the claim should define and clearly state as to what the improved bioluminescent assay is being compared. Put another way, an improved bioluminescent assay using the protein of claim 67 in comparison to a bioluminescent assay using what protein?

[b] Claim 85 is unclear in the recitation of "vector...transformed in a cell" as claim 84 is not drawn to a vector, but instead further limits the nucleic acid of claim 83 to being in a vector. Even if claim 83 was drawn to "a vector," claim 85 is confusing in that it is unclear as to how the "vector of claim 84" is "transformed in a cell" such that a skilled artisan would recognize the scope of "transformed" vectors. It is suggested that applicant clarify the meaning of the claim by, for example, amending claim 84 to recite

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“[a] vector comprising the nucleic acid of claim 83” and amending claim 85 to recite “[a]n isolated cell comprising the vector of claim 84.”

Claim Rejections - 35 USC § 112, First Paragraph

[13] The written description rejection of claims 31-35, 37-38, 51-62, and 64-66 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's amendment to cancel the claims. The rejection is herein applied to new claims 67-85. The written description rejection of claims 67-85 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the genus of claimed proteins and nucleic acids is described by both structural and functional limitations as encompassed by the claims and the specification discloses a number of representative examples of the claimed genus sufficient to show possession. Applicant points to the “Revised Interim Written Description Guidelines Training Materials” which states that a single representative species may be sufficient to describe a genus (p. 31, top). Applicant further points to Example 14 at pp. 53-55, which sets forth the following claim: “[a] protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A→ B” and states that a single disclosed species is sufficient to describe the claimed genus. By analogy, applicant argues, the disclosed species describes the claimed genus of proteins and nucleic acids. Applicant

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argues the term "similarity" is described in the specification and a skilled artisan would recognize how to determine those sequences which have the recited "similarity."

Applicant's argument is not found persuasive. The examiner acknowledges that the genus of claimed proteins and nucleic acids is described by the structural feature of being 90% similar to SEQ ID NO:37, having mutation at position 214, and having the function of luciferase and increased thermostability. The issue is whether the disclosed species adequately describe all members of the claimed genus, which encompasses any protein from any source having the recited 90% similarity to SEQ ID NO:37 and the recited functional characteristics. While applicant argues that by analogy to Example 14, the claimed genus is adequately described. However, in contrast to the instant claims which are drawn to variants having "at least 90% similarity to...SEQ ID NO:37," the structures of the proteins of the claim of Example 14 are limited to those that are "at least 95% identical to SEQ ID NO:3." Thus, there are at least two differences between the Example 14 claim and the instant claims: 1) the number limitation, *i.e.*, 90% and 95%, and 2) the method of sequence comparison, *i.e.*, identity and similarity. Thus, contrary to applicant's argument, the instant claims are not analogous to Example 14 of the Guidelines. Further, because the claims recite "similarity," the examiner maintains that the members of the genus of claimed proteins and nucleic acids are widely variant, which is undisputed by applicant. While the examiner acknowledges applicant's remark that a single species *may* be sufficient to describe a genus, MPEP § 2163 makes clear that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one

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species within the genus" and the Court recognizes that the biological arts are unpredictable. See *Mycogen Plant Science Inc. v. Monsanto Co.*, 58 USPQ2d 1030 (CAFC 2001).

Thus, at least for the reasons of record and the reasons stated above, the examiner maintains that the specification fails to adequately describe all members of the claimed genus of proteins and nucleic acids as encompassed by the claims.

[14] The scope of enablement rejection of claims 31-35, 37-38, 51-62, and 64-66 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's amendment to cancel the claims. The rejection is herein applied to new claims 67-85. The scope of enablement rejection of claims 67-85 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues: 1) numerous working examples of the claimed invention are disclosed; 2) sufficient guidance is disclosed in the specification regarding the making, testing, and using of variants encompassed by the claims to enable a skilled artisan to make the use the full scope of the claimed invention without undue experimentation; 3) the examiner focuses only on the level of predictability in the art instead of considering all relevant Factors of *In re Wands*; 4) inventions in the biological sciences may have "some unpredictability" as evidenced by issued US patents and the "Revised Interim Written Description Guidelines Training Materials."

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Applicants' argument is not found persuasive. While it is acknowledged that the examiner's remarks addressing the instant rejection in the 9/19/2005 Office action focus on the level of predictability in the art, this was necessitated by applicant's arguments in the response filed on 4/15/2005, which also focus on this Factor of *In re Wands*.

Contrary to applicant's argument and in accordance with MPEP § 2164.04, which states "it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims," the examiner *has* addressed all relevant Factors of *In re Wands* in a prior Office action (see particularly pp. 12-16 of the Office action mailed on 12/15/2004). In this case, the claims are so broad as to encompass all "recombinant" proteins having "at least 90% similarity" to SEQ ID NO:37, mutation at position 214, and having luciferase activity and increased thermostability. In this case, the claims encompass numerous variants of SEQ ID NO:37 that have the recited luciferase activity and increased thermostability. The examiner acknowledges the specification's disclosure of the working examples of SEQ ID NO:37 with mutation at position 214 and optionally position 215, 232, and/or 354 and general guidance for creating variants and methods for testing the resulting variants for luciferase activity and increased thermostability. However, as noted in a prior Office action, the functional effect(s) of altering the amino acid sequence of a polypeptide are *highly* unpredictable, which is

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undisputed by applicant, and is supported by the prior art (see p. 15 of the Office action mailed on and p. 9 of the Office action mailed on 9/19/2005). The level of unpredictability is further compounded by the requirement of the claims that require not only the encoded protein have luciferase activity, but also that it have increased thermostability. Neither the specification nor the prior art provide any expectation that the corresponding mutation at position 214 of SEQ ID NO:37 in other luciferase polypeptides from other sources will have the desired effect of: a) maintaining luciferase activity and b) increasing thermostability and, other than the specifically disclosed working examples, there is no expectation that additional mutations will not deleteriously affect luciferase activity and/or thermostability. The high level of unpredictability is further supported by the references of Sung et al. (*Photochem Photobiol* 68:749-753, 1998, abstract only) and Law et al. (*Biochem J* [Epub ahead of print], 3/21/2006, abstract only), which were published after the earliest effective filing date of the instant application. Sung et al. discloses that mutations at the first 11 amino acids of the N-terminus of *P. pyralis* luciferase have are important to the stability of the enzyme, showing that various N-terminal substitutions significantly reduce luciferase activity, while Law et al. discloses that substitution of position 14 of *P. pyralis* luciferase improves thermostability and retain the specific activity of the wild-type enzyme. While methods of altering the sequence of a polypeptide were known in the art at the time of the invention, it was not routine to make all variant proteins as encompassed by the claims having a *substantial* number of modifications without the necessary guidance and screen those variants for those having luciferase activity and increased

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thermostability as encompassed by the claims. Thus, in view of the broad scope of the claims, the lack of guidance and working examples, the high level of unpredictability, and the amount of non-routine experimentation required, the examiner maintains the position that undue experimentation is required to make the full scope of claimed proteins and nucleic acids.

Regarding applicant's argument relying upon issued US patents, applicant is reminded that each application is examined on its merits. That a claim has been determined to satisfy the enablement requirement is not only a consideration of the claim language itself, but also the underlying facts of each application. Regarding applicant's argument relying upon the "Revised Interim Written Description Guidelines Training Materials" for demonstrating enablement, it is noted that MPEP § 2164 states, "[t]he enablement requirement of 35 U.S.C. 112, first paragraph, is separate and distinct from the description requirement."

Claim Rejections - 35 USC § 102

[15] The rejection of claims 31-32, 34-35, 37, 51-52, 60-62, and 64-65 under 35 U.S.C. 102(b) as being anticipated by Database EMBL Accession Number D25415 as evidenced by Wood et al. (US Patent Application Publication 2003/0068801) is withdrawn in view of applicant's amendment to cancel the claims. The rejection does not apply to newly added claims 67-85 in view of the amendment to limit the polypeptide to having at least 90% similarity to SEQ ID NO:37.

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[16] The rejection of claims 31-32, 34-35, 37, 51-54, 57-62, and 64-66 under 35 U.S.C. 102(e) as being anticipated by Wood et al. (US Patent Application Publication 2003/0068801) is withdrawn in view of applicant's amendment to cancel the claims. The rejection does not apply to newly added claims 67-85 in view of the amendment to limit the polypeptide to having at least 90% similarity to SEQ ID NO:37.

Claim Rejections - 35 USC § 103

[17] The rejection of claim(s) 55-56 under 35 U.S.C. 103(a) as being unpatentable over Firoozabady et al. (US Patent 5,480,789) in view of Wood et al. is withdrawn in view of applicant's amendment to cancel the claims. The rejection does not apply to newly added claims 67-85 in view of the amendment to limit the polypeptide to having at least 90% similarity to SEQ ID NO:37.

Double Patenting Rejection(s)

[18] The provisional obviousness-type double patenting rejection of claims 1-5, 7-8, and 21-23 as being unpatentable over claims 1-4, 6-10, 14, 17-19 and 6-23 of co-pending Application No. 10/111,723 is withdrawn in view of applicant's amendment to cancel the claims. The provisional rejection is herein applied to new claims 67-85 for the reasons of record. The provisional rejection was fully explained in a prior Office action.

Conclusion

[19] Status of the claims:

Claims 67-85 are pending.

Claims 67-85 are rejected.

No claim is in condition for allowance.


Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656